REMARKS

The previous rejections of various claims under 35 U.S.C. 112, second paragraph, have been withdrawn in view of Applicants' earlier amendments. The rejection of claim 13 under 35 U.S.C. 101 has been withdrawn in view of the cancellation of this claim. The rejection of the remaining claims 1 - 12 under 35 U.S.C. 103 (a) as unpatentable over Hester et al in view of Nair et al. and as unpatentable over Yoshida et al. in view of Nair et al. remain. Applicants respectfully request reconsideration of these rejections in view of the amendments made herein and in view of the remarks below.

THE REJECTION FOR INHERENCY AND THE NON-PATENTABILITY OF A NEW FUNCTION OR UNKNOWN PROPERTY

The Office states that Hester's method or Yoshida's method inherently treats or protects osteoporosis, bone resorption, or other bone disease in a vertebrate mammal because the steps described in Hester or Yoshida are the same as the instant method steps. It is apparently the Office's position that because the compounds of the claims of this application have been administered to patients suffering from bacterial infections and these patients may have also been suffering from osteoporosis, bone resorption, or suffering from other bone diseases including bone diseases associated with bacteria, the treatment of these conditions would have "inherently" resulted from the treatment of the co-morbid bacterial infections.

Applicants submit that inherency of a result does not render obvious the result. Inherency is not relevant unless one of ordinary skill in the art would have appreciated or recognized the result. *In re Naylor*, 152 U.S.P.Q. 106 (CCPA 1966). Thus here, Applicants submit that while the compounds described in the claims of this application may have been previously administered to patients suffering from various bacterial infections, and in some instances some of these patients may have also been suffering from certain diseases characterized by loss of bone tissue and such patients likely would have had some increase in bone tissue resulting from the administration of these agents, such result was not appreciated nor recognized. Rather only the resulting treatment

of the bacterial infection was noted in the prior art. As such, Applicants submit that the use of the compounds described in the claims of this application to treat osteoporosis, bone resorption or other bone diseases characterized by the need to enhance bone formation is not rendered obvious by the use of the same compounds to treat bacterial infections.

The Office relies on *In re Best*, 195 U.S.P.Q. 430, 433 (CCPA 1977) quoting a passage from *In re Swinehart*, 169 U.S.P.Q. 226 (CCPA 1971) to support its position that the discovery of a new property, inherently possessed by things in the prior art, is not patentable and is obvious. Applicants agree that newly discovered properties do not render the substance patentable. But Applicants submit the discovery of a new use may be properly claimed as a process (method) of using an old substance with other known uses. This is the basis of method of use claims.

The Office further relies on MPEP 2112.01 to support its position. But this section, entitled "Composition, Product, and Apparatus Claims" deals with claims directed to compositions not to a nearly discovered use of an old substance. Here Applicants are claiming a method of using various previously known compounds, not the compounds per se. Applicants note that in MPEP section 2112.02 there is a subsection entitled "Process of Use - New and Unobvious Uses of Old Structures and Compositions May be Patentable." This is what Applicants seek to do. Applicants have discovered a new use of an old substance and have presented claims to a process (method) of using the old substance for the newly discovered use. This clearly is patentable.

THE NONOBVIOUSNESS OF ENHANCEMENT OF BONE FORMATION

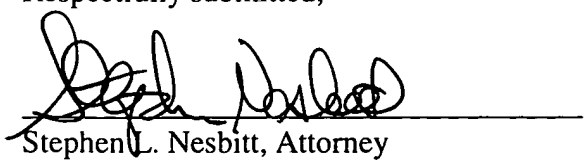
Applicants note that by way of amendment of claims 1 and 7 the invention claimed in this application is limited to the treatment of 1) osteoporosis, 2) bone resorption or 3) other bone diseases characterized by the need to enhance bone formation. Applicants note that clearly the prior art does not teach or suggest that osteoporosis or bone resorption can be treated with the compounds described in the claims of this application. Both osteoporosis and bone resorption are not reported to have a bacterial basis either in the Nair reference or otherwise. Some of the diseases characterized by the term "bone diseases" can have a bacterial causation but by way of

the amendments above, Applicants' claims are now clearly limited to and are directed only to bone diseases characterized by the need to enhance bone formation. This, Applicants submit, clearly distinguishes the scope of the present claims from the prior art treatment of bone infections to the treatment of diseases of the bone requiring enhancement of bone formation. Applicants thus distinguish the prior art that describes the use of certain compounds to prevent further loss of bone tissue caused by bacterial infection by treatment of the bone infection from the instantly claimed invention where the use of certain compounds is claimed for the enhancement of bone formation. Thus while some bacterial infections, i.e. bone diseases, result in loss of bone tissue and the patients suffering from these infections clearly would benefit from enhanced bone formation, Applicants submit that one of ordinary skill in the art would not have considered this obvious and thus Applicants submit that this rejection should be reconsidered and withdrawn.

APPLICANTS' RESULTS ON USE OF COMPOUNDS

The Office states that the specification at pages 44-45 does not provide evidence of nonobviousness or unexpected results over the prior art. Applicants have not relied on the data presented in the application as evidence of the nonobviousness of the presently claimed invention. Indeed, Applicants submit that it is not necessary to present such data because the Office has not established a prima facie case of obviousness for the reasons outlined above.

Respectfully submitted,



Date: November 6, 2002

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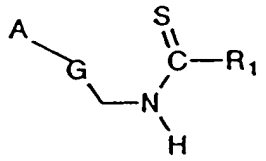
Version with markings to show changes made

In the claims:

Claim 1 has been amended as follows:

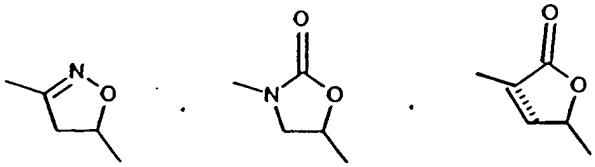
1. (amended) A method of treating or preventing osteoporosis, bone resorption, or other bone disease characterized by the need to enhance bone formation in a vertebrate mammal[,] in need thereof comprising the [step of] administering to [a] the vertebrate mammal [in need of such treatment,] an effective amount of a compound of formula I



I

or pharmaceutical acceptable salts thereof wherein:

G is



R_1 is

a) H,

b) NH_2,

c) NH-C_{1-4} alkyl,

d) C_{1-4} alkyl,

e) -OC_{1-4} alkyl,

f) -S C_{1-4} alkyl,

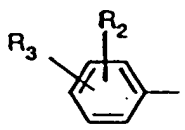
g) C_{1-4} alkyl substituted with 1-3 F, 1-2 Cl, CN or -$COOC_{1-4}$ alkyl,

h) C_{3-6} cycloalkyl,

i) $N(C_{1-4}$ alkyl$)_2$ or

j) $N(CH_2)_{2-5}$;

A is

a) 

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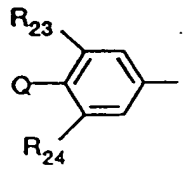
b) 

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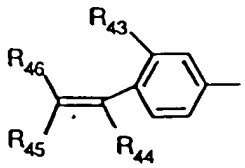
c) 

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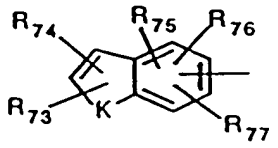
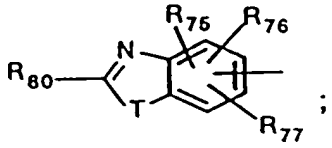
d) a 5-membered heteroaromatic moiety having one to three atoms selected from the group consisting of S, N, and O,
wherein the 5-membered heteroaromatic moiety is bonded via a carbon atom,
wherein the 5-membered heteroaromatic moiety can additionally have a fused-on benzene or naphthyl ring,
wherein the heteroaromatic moiety is optionally substituted with one to three R_{48},

e) a 6-membered heteroaromatic moiety having at least one nitrogen atom,
wherein the heteroaromatic moiety is bonded via a carbon atom,
wherein the 6-membered heteroaromatic moiety can additionally have a fused-on benzene or naphthyl ring,
wherein the heteroaromatic moiety is optionally substituted with one to three R_{55},

f) a β-carbolin-3-yl, or indolizinyl bonded via the 6-membered ring, optionally substituted with one to three R_{65},

g)  , or

h)  ;

wherein R_2 is

a) H,

b) F,

c) Cl,

d) Br,

e) C_{1-3} alkyl,

f) NO_2, or

g) R_2 and R_3 taken together are $-O-(CH_2)_h-O-$;

R_3 is

a) $-S(=O)_i R_4$,

b) $-S(=O)_2-N=S(O)_j R_5 R_6$,

c) $-SC(=O)R_7$,

d) $-C(=O)R_8$,

e) $-C(=O)R_9$,

f) $-C(=O)NR_{10}R_{11}$,

g) $-C(=NR_{12})R_8$,

h) $-C(R_8)(R_{11})-OR_{13}$,

i) $-C(R_9)(R_{11})-OR_{13}$,

j) $-C(R_8)(R_{11})-OC(=O)R_{13}$,

k) $-C(R_9)(R_{11})-OC(=O)R_{13}$,

l) $-NR_{10}R_{11}$,

m) $-N(R_{10})-C(=O)R_7$,

n) $-N(R_{10})-S(=O)_iR_7$,

o) $-C(OR_{14})(OR_{15})R_8$,

p) $-C(R_8)(R_{16})-NR_{10}R_{11}$, or

q) C_{1-8} alkyl substituted with one or more =O other than at alpha position, $-S(=O)_iR_{17}$, $-NR_{10}R_{11}$, C_{2-6} alkenyl, or C_{2-6} alkynyl;

R_4 is

a) C_{1-4} alkyl optionally substituted with one or more halos, OH, CN, $NR_{10}R_{11}$, or $-CO_2R_{13}$,

b) C_{2-4} alkenyl,

c) $-NR_{16}R_{18}$,

d) $-N_3$,

e) $-NHC(=O)R_7$,

f) $-NR_{20}C(=O)R_7$,

g) $-N(R_{19})_2$,

h) $-NR_{16}R_{19}$, or

i) $-NR_{19}R_{20}$,

R_5 and R_6 at each occurrence are the same or different and are

a) C_{1-2} alkyl, or

b) R_5 and R_6 taken together are $-(CH_2)_k-$;

R_7 is C_{1-4} alkyl optionally substituted with one or more halos;

R_8 is

a) H, or

b) C_{1-8} alkyl optionally substituted with one or more halos, or C_{3-8} cycloalkyl;

R_9 is C_{1-4} alkyl substituted with one or more

a) $-S(=O)R_{17}$,

b) $-OR_{13}$,

c) $-OC(=O)R_{13}$,

d) $-NR_{10}R_{11}$, or

e) C_{1-6} alkenyl optionally substituted with CHO;

R_{10} and R_{11} at each occurrence are the same or different and are

a) H,

b) C_{1-4} alkyl, or

c) C_{3-8} cycloalkyl;

R_{12} is

a) $-NR_{10}R_{11}$,

b) $-OR_{10}$; or

c) $-NHC(=O)R_{10}$;

R_{13} is

a) H, or

b) C_{1-4} alkyl;

R_{14} and R_{15} at each occurrence are the same or different and are

a) C_{1-4} alkyl, or

b) R_{14} and R_{15} taken together are $-(CH)_1-$;

R_{16} is

a) H,

b) C_{1-4} alkyl, or

c) C_{3-8} cycloalkyl;

R_{17} is

a) C_{1-4} alkyl, or

b) C_{3-8} cycloalkyl;

R_{18} is

a) H,

b) C_{1-4} alkyl,

c) C_{2-4} alkenyl,

d) C_{3-4} cycloalkyl,

e) $-OR_{13}$ or

f) $-NR_{21}R_{22}$;

R_{19} is

a) Cl,

b) Br, or

c) I;

R_{20} is a physiologically acceptable cation;

R_{21} and R_{22} at each occurrence are the same or different and are

a) H,

b) C_{1-4} alkyl, or

c) $-NR_{21}R_{22}$ taken together are $-(CH_2)_m-$;

wherein R_{23} and R_{24} at each occurrence are the same or different and are

a) H,

b) F,

c) Cl,

d) C_{1-2} alkyl,

e) CN

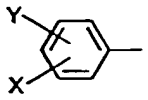
f) OH,

g) C_{1-2} alkoxy,

h) nitro, or

i) amino;

Q is

a) 

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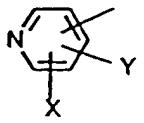
b) 

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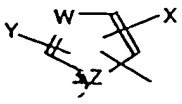
c) 

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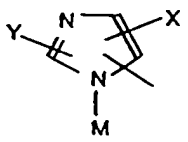
d) 

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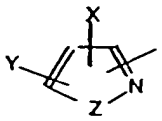
e) 

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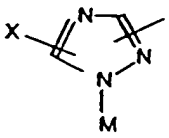
f) 

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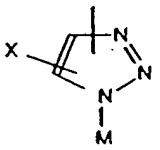
g) 

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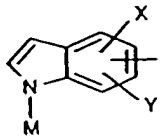
h) 

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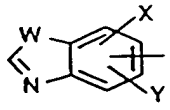
i) 

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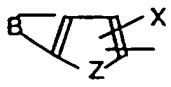
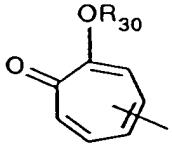
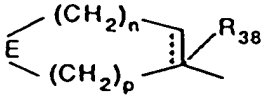
j) 

k) 

l) 

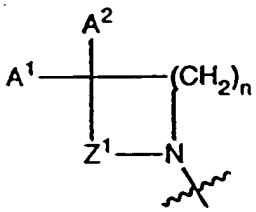
m) a diazinyl group optionally substituted with X and Y,

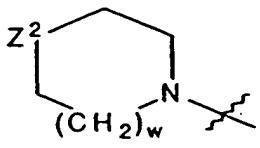
n) a triazinyl group optionally substituted with X and Y,

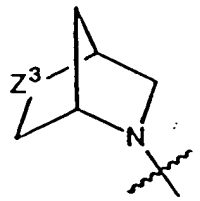
o) a quinolinyl group optionally substituted with X and Y,

p) a quinoxalinyl group optionally substituted with X and Y,

q) a naphthyridinyl group optionally substituted with X and Y,

r) 

s) 

t) 

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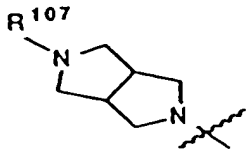
u) 

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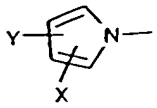
v) 

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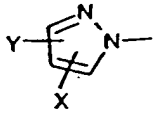
w) 

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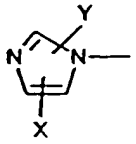
x) 

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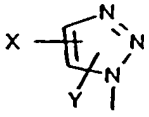
y) 

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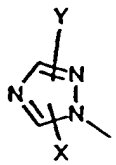
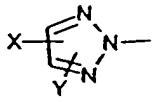
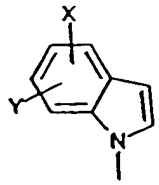
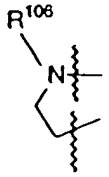
z)  ,

aa)  ,

bb)  or,

Q and R_{24} taken together are

 ,

wherein Z^1 is

a) $-CH_2-$,

b) $-CH(R^{104})-CH_2-$,

c) -C(O)-, or

d) $-CH_2CH_2CH_2-$;

wherein Z^2 is

a) $-O_2S-$,

b) -O-,

c) $-N(R^{107})-$,

d) -OS-, or

e) -S-;

wherein Z^3 is

a) $-O_2S-$,

b) -O-,

c) -OS-, or

d) -S-;

wherein A^1 is

a) H-, or

b) CH_3;

wherein A^2 is

a) H-,

b) HO-,

c) CH_3-,

d) CH_3O-,

e) $R^{102}O-CH_2-C(O)-NH-$

f) $R^{103}O-C(O)-NH-$,

g) (C_1-C_2)alkyl-O-C(O)-,

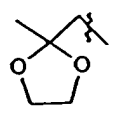
h) $HO-CH_2-$,

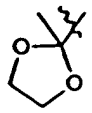
i) CH_3O-NH-,

j) (C_1-C_3)alkyl-O_2C-

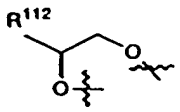
k) $CH_3-C(O)-$,

l) $CH_3-C(O)-CH_2-$,

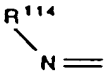
m)  , or

n)  ,

A^1 and A^2 taken together are:

a)  ,

b)  , or

c)  ;

wherein R^{102} is

a) H-,

b) CH_3-,

c) phenyl-CH_2-, or

d) $CH_3C(O)$-;

wherein R^{103} is

a) $(C_1$-$C_3)$alkyl-, or

b) phenyl-;

wherein R^{104} is

a) H-, or

b) HO-;

wherein R^{105} is

a) H-,

b) $(C_1$-$C_3)$alkyl-,

c) $CH_2 = CH$-CH_2-, or

d) CH_3-O-$(CH_2)_2$-;

wherein R^{106} is

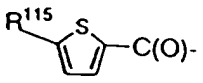
a) CH_3-C(O)-,

b) H-C(O)-,

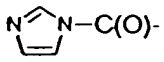
c) Cl_2CH-C(O)-,

d) $HOCH_2$-C(O)-,

e) CH_3SO_2-,

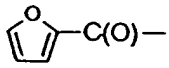
f)  ,

g) $F_2CHC(O)$-,

h)  ,

i) H_3C-C(O)-O-CH_2-C(O)-,

j) H-C(O)-O-CH_2-C(O)-,

k)  ,

l) HC≡C-CH_2O-CH_2-C(O)-, or

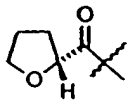
m) phenyl-CH_2-O-CH_2-C(O)-;

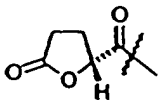
wherein R^{107} is

a) R^{102}O-C(R^{110})(R^{111})-C(O)-,

b) R^{103}O-C(O)-,

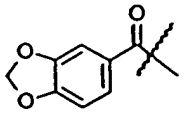
c) R^{108}-C(O)-,

d)  ,

e)  ,

f) H_3C-C(O)-$(CH_2)_2$-C(O)-,

g) R^{109}-SO_2-,

h)  ,

i) $HO\text{-}CH_2\text{-}C(O)\text{-}$,

j) $R^{116}\text{-}(CH_2)_2\text{-}$,

k) $R^{113}\text{-}C(O)\text{-}O\text{-}CH_2\text{-}C(O)\text{-}$,

l) $(CH_3)_2N\text{-}CH_2\text{-}C(O)\text{-}NH\text{-}$,

m) $NC\text{-}CH_2\text{-}$,

n) $F_2\text{-}CH\text{-}CH_2\text{-}$, or

o) $R^{150}R^{151}NSO_2$

wherein R^{108} is

a) H-,

b) $(C_1\text{-}C_4)$alkyl,

c) aryl $\text{-}(CH_2)_p$,

d) $ClH_2C\text{-}$,

e) $Cl_2HC\text{-}$,

f) $FH_2C\text{-}$,

g) $F_2HC\text{-}$,

h) $(C_3\text{-}C_6)$cycloalkyl, or

i) $CNCH_2\text{-}$.

wherein R^{109} is

a) alkyl$C_1\text{-}C_4$,

b) $\text{-}CH_2Cl$

c) $\text{-}CH_2CH{=}CH_2$,

d) aryl, or

e) $\text{-}CH_2CN$;

wherein R^{110} and R^{111} are independently

a) H-,

b) $CH_3\text{-}$; or

wherein R^{112} is

a) H-,

b) $CH_3O\text{-}CH_2O\text{-}CH_2\text{-}$, or

c) $HOCH_2\text{-}$;

wherein R^{113} is

a) CH_3-,

b) $HOCH_2$-,

c) $(CH_3)_2N$-phenyl, or

d) $(CH_3)_2N$-CH_2-;

wherein R^{114} is

a) HO-,

b) CH_3O-,

c) H_2N-,

d) CH_3O-C(O)-O-,

e) CH_3-C(O)-O-CH_2-C(O)-O-,

f) phenyl-CH_2-O-CH_2-C(O)-O-,

g) HO-$(CH_2)_2$-O-,

h) CH_3O-CH_2-O-$(CH_2)_2$-O-, or

i) CH_3O-CH_2-O-;wherein R^{113} is

a) CH_3-,

b) $HOCH_2$-,

c) $(CH_3)_2N$-phenyl, or

d) $(CH_3)_2N$-CH_2-;

wherein R^{115} is

a) H-, or

b) Cl-;

wherein R^{116} is

a) HO-

b) CH_3O-, or

c) F;

wherein R^{150} and R^{151} are each H or alkyl C_1-C_4 or R^{150} and R^{151} taken together with the nitrogen atom to which each is attached form a monocyclic heterocyclic ring having from 3 to 6 carbon atoms;

B is an unsaturated 4-atom linker having one nitrogen and three carbons;

M is

a) H,

b) C_{1-6} alkyl,

c) C_{3-6} cycloalkyl,

d) $-(CH_2)_mOR_{13}$, or

e) $-(CH_2)_h-NR_{21}R_{22}$;

Z is

a) O,

b) S, or

c) NM;

W is

a) CH,

b) N, or

c) S or O when Z is NM;

Y is

a) H,

b) F,

c) Cl,

d) Br,

e) C_{1-3} alkyl, or

f) NO_2;

X is

a) H,

b) -CN,

c) OR_{27},

d) halo,

e) NO_2,

f) tetrazoyl,

g) -SH,

h) $-S(=O)_iR_4$,

i) $-S(=O)_2-N=S(O)_jR_5R_6$,

j) $-SC(=O)R_7$,

k) $-C(=O)R_{25}$,

l) $-C(=O)NR_{27}R_{28}$,

m) $-C(=NR_{29})R_{25}$,

n) $-C(R_{25})(R_{28})-OR_{13}$,

o) $-C(R_{25})(R_{28})-OC(=O)R_{13}$,

p) $-C(R_{28})(OR_{13})-(CH_2)_h-NR_{27}R_{28}$,

q) $-NR_{27}R_{28}$,

r) $-N(R_{27})C(=O)R_7$,

s) $-N(R_{27})-S(=O)_iR_7$,

t) $-C(OR_{14})(OR_{15})R_{28}$,

u) $-C(R_{25})(R_{16})-NR_{27}R_{26}$, or

v) C_{1-8} alkyl substituted with one or more halos, OH, =O other than at alpha position, $-S(=O)_iR_{17}$, $-NR_{27}R_{28}$, C_{2-5} alkenyl, C_{2-5} alkynyl, or C_{3-8} cycloalkyl;

R_4, R_5, R_6, R_7, R_{13}, R_{14}, R_{15}, R_{16}, and R_{17} are the same as defined above;

R_{25} is

a) H,

b) C_{1-8} alkyl optionally substituted with one or more halos, C_{3-8} cycloalkyl, C_{1-4} alkyl substituted with one or more of $-S(=O)_iR_{17}$, $-OR_{13}$, or $OC(=O)R_{13}$, $NR_{27}R_{28}$, or

c) C_{2-6} alkenyl optionally substituted with CHO, or CO_2R_{13};

R_{26} is

a) R_{28}, or

b) $NR_{27}N_{28}$;

R_{27} and R_{28} at each occurrence are the same or different and are

a) H,

b) C_{1-8} alkyl,

c) C_{3-8} cycloalkyl,

d) $-(CH_2)_mOR_{13}$,

e) $-(CH_2)_h-NR_{21}R_{22}$, or

f) R_{27} and R_{28} taken together are $-(CH_2)_2O(CH_2)_2-$, $-(CH_2)_hCH(COR_7)-$, or $-(CH_2)_2N(CH_2)_2(R_7)$;

R_{29} is

a) $-NR_{27}R_{28}$,

b) $-OR_{27}$, or

c) $-NHC(=O)R_{26}$;

wherein R_{30} is

a) H,

b) C_{1-8} alkyl optionally substituted with one or more halos, or

c) C_{1-8} alkyl optionally substituted with one or more OH, or C_{1-6} alkoxy;

wherein E is

a) NR_{39},

b) $-S(=O)_i$, or

c) O;

R_{38} is

a) H,

b) C_{1-6} alkyl,

c) $-(CH_2)_q$-aryl, or

d) halo;

R_{39} is

a) H,

b) C_{1-6} alkyl optionally substituted with one or more OH, halo, or -CN,

c) $-(CH_2)_q$-aryl,

d) $-CO_2R_{40}$,

e) $-COR_{41}$,

f) $-C(=O)-(CH_2)_q-C(=O)R_{40}$,

g) $-S(=O)_2-C_{1-6}$ alkyl,

h) $-S(=O)_2-(CH_2)_q$-aryl, or

i) $-(C=O)_j$-Het;

R_{40} is

a) H,

b) C_{1-6} alkyl optionally substituted with one or more OH, halo, or -CN,

c) $-(CH_2)_q$-aryl, or

d) $-(CH_2)_q-OR_{42}$;

R_{41} is

a) C_{1-6} alkyl optionally substituted with one or more OH, halo, or -CN,

b) $-(CH_2)_q$-aryl, or

c) $-(CH_2)_q-OR_{42}$;

R_{42} is

a) H,

b) C_{1-6} alkyl,

c) $-(CH_2)_q$-aryl, or

d) $-C(=O)-C_{1-6}$ alkyl;

aryl is

a) phenyl,

b) pyridyl, or

c) napthyl; a to c optionally substituted with one or more halo, -CN, OH, SH, C_{1-6} alkyl, C_{1-6} alkoxy, or C_{1-6} alkylthio;

wherein R_{43} is

a) H,

b) C_{1-2} alkyl,

c) F, or

d) OH;

R_{44} is

a) H,

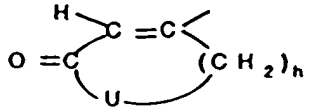
b) CF_3,

c) C_{1-3} alkyl optionally substituted with one or more halo,

d) phenyl optionally substituted with one or more halo,

e) R_{44} and R_{45} taken together are a 5-, 6-, or 7-membered ring of the formula,

or



f) R_{44} and R_{45} taken together are $-(CH_2)_k-$, when R_{46} is an electron-withdrawing group;

R_{45} and R_{46} at each occurrence are the same or different and are

a) an electron-withdrawing group,

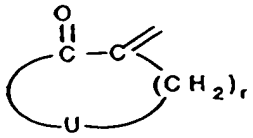
b) H,

c) CF_3,

d) C_{1-3} alkyl optionally substituted with one halo,

e) phenyl, provided at least one of R_{45} or R_{46} is an electron-withdrawing group, or

f) R_{45} and R_{46} taken together are a 5-, 6-, 7-membered ring of the formula



;

U is

a) CH_2,

b) O,

c) S, or

d) NR_{47};

R_{47} is

a) H, or

b) C_{1-5} alkyl;

wherein R_{48} is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) $-NO_2$,

h) C_{1-6} alkoxy,

i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

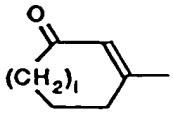
l) $-NR_{49}R_{50}$,

m) C_{1-6} alkyl optionally substituted with OH, C_{1-5} alkoxy, C_{1-5} acyl, or $-NR_{49}R_{50}$,

n) C_{2-8} alkenylphenyl optionally substituted with one or two R_{51},

o) phenyl optionally substituted with one or two R_{51},

p) a 5-, or 6-membered (un)saturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with one or two R_{51}, or

q)  ;

R_{49} and R_{50} at each occurrence are the same or different and are

a) H,

b) C_{1-4} alkyl,

c) C_{5-6} cycloalkyl, or

d) R_{49} and R_{50} taken together with the nitrogen atom is a 5-, 6-membered saturated heterocyclic moiety which optionally has a further hetero atom selected from the group consisting of S, N, and O, and can in turn be optionally substituted with, including on the further nitrogen atom, C_{1-3} alkyl, or C_{1-3} acyl;

R_{51} is

a) carboxyl,
b) halo,
c) -CN,
d) mercapto,
e) formyl,
f) CF_3,
g) $-NO_2$,
h) C_{1-6} alkoxy,
i) C_{1-6} alkoxycarbonyl,
j) C_{1-6} alkythio,
k) C_{1-6} acyl,
l) C_{1-6} alkyl optionally substituted with OH, C_{1-6} alkoxy, C_{1-6} acyl, or $-NR_{49}R_{50}$,
m) phenyl,
n) $-C(=O)NR_{52}R_{53}$,
o) $-NR_{49}R_{50}$,
p) $-N(R_{52})(-SO_2R_{54})$,
q) $-SO_2-NR_{52}R_{53}$, or
r) $-S(=O)_iR_{54}$;

R_{52} and R_{53} at each occurrence are the same or different and are

a) H,
b) C_{1-6} alkyl, or
c) phenyl;

R_{54} is

a) C_{1-4} alkyl, or

b) phenyl optionally substituted with C_{1-4} alkyl;

wherein R_{55} is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) $-NO_2$,

h) C_{1-6} alkoxy,

i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio

k) C_{1-6} acyl,

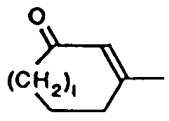
l) $-NR_{56}R_{57}$,

m) C_{1-6} alkyl optionally substituted with OH, C_{1-5} alkoxy, C_{1-5} acyl, or $-NR_{56}R_{57}$,

n) C_{2-8} alkenylphenyl optionally substituted with one or two R_{58},

o) phenyl optionally substituted with one or two R_{58},

p) a 5- or 6-membered (un)saturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with one or two R_{58}, or

q)  ;

R_{56} and R_{57} at each occurrence are the same or different and are

a) H,

b) formyl,

c) C_{1-4} alkyl,

d) C_{1-4} acyl,

e) phenyl,

f) C_{3-6} cycloalkyl, or

g) R_{66} and R_{67} taken together with the nitrogen atom is a 5-, 6-membered saturated heterocyclic moiety which optionally has a further hetero atom selected from the group consisting of S, N, and O, and can in turn be optionally substituted with, including on the further nitrogen atom, phenyl, pyrimidyl, C_{1-3} alkyl, or C_{1-3} acyl;

R_{58} is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) $-NO_2$,

h) C_{1-6} alkoxy,

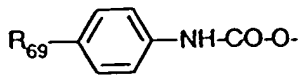
i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

l) phenyl,

m) C_{1-6} alkyl optionally substituted with OH, azido, C_{1-5} alkoxy, C_{1-5} acyl, $-NR_{65}R_{66}$, $-SR_{67}$, $-O-SO_2R_{68}$, or



,

n) $-C(=O)NR_{69}\ R_{60}$,

o) $-NR_{66}R_{67}$,

p) $-N(R_{69})(-SO_2R_{64})$,

q) $-SO_2-NR_{59}R_{60}$,

r) $-S(=O)_iR_{64}$,

s) $-CH=N-R_{61}$, or

t) $-CH(OH)-SO_3R_{64}$;

R_{64} is the same as defined above;

R_{59} and R_{60} at each occurrence are the same or different and are

a) H,

b) C_{1-6} alkyl,

c) phenyl, or

d) tolyl;

R_{61} is

a) OH,

b) benzyloxy,

c) $-NH-C(=O)-NH_2$,

d) $-NH-C(=S)-NH_2$, or

e) $-NH-C(=NH)-NR_{62}R_{63}$;

R_{62} and R_{63} at each occurrence are the same or different and are

a) H, or

b) C_{1-4} alkyl optionally substituted with phenyl or pyridyl;

R_{64} is

a) H, or

b) a sodium ion;

R_{65} and R_{66} at each occurrence are the same or different and are

a) H,

b) formyl,

c) C_{1-4} alkyl,

d) C_{1-4} acyl,

e) phenyl,

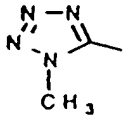
f) C_{3-6} cycloalkyl,

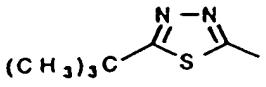
g) R_{65} and R_{66} taken together are a 5-, 6-membered saturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with, including on the nitrogen atom, phenyl, pyrimidyl, C_{1-3} alkyl, or C_{1-3} acyl,

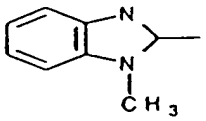
h) $-P(O)(OR_{70})(OR_{71})$, or

i) $-SO_2-R_{72}$;

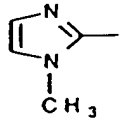
R_{67} is







or



R_{68} is C_{1-3} alkyl;

R_{69} is

a) C_{1-6} alkoxycarbonyl, or

b) carboxyl;

R_{70} and R_{71} at each occurrence are the same or different and are

a) H, or

b) C_{1-3} alkyl;

R_{72} is

a) methyl,

b) phenyl, or

c) tolyl;

wherein K is

a) O, or

b) S;

R_{73}, R_{74}, R_{75}, R_{76}, and R_{77} at each occurrence are the same or different and are

a) H,

b) carboxyl,

c) halo,

d) -CN,

e) mercapto,

f) formyl,

g) CF_3,

h) $-NO_2$,

i) C_{1-6} alkoxy,

j) C_{1-6} alkoxycarbonyl,

k) C_{1-6} alkythio,

l) C_{1-6} acyl,

m) $-NR_{78}R_{79}$,

n) C_{1-6} alkyl optionally substituted with OH, C_{1-5} alkoxy, C_{1-5} acyl, $-NR_{78}R_{79}$, -N(phenyl)(CH_2-CH_2-OH), -O-CH(CH_3)(OCH_2CH_3), or -O-phenyl-[para-NHC(=O)CH_3],

o) C_{2-8} alkenylphenyl optionally substituted with R_{51},

p) phenyl optionally substituted with R_{51}, or

q) a 5-, or 6-membered (un)saturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with R_{51};

R_{51} is the same as defined above;

R_{78} and R_{79} at each occurrence are the same or different and are

a) H,

b) C_{1-4} alkyl,

c) phenyl, or

d) R_{78} and R_{79} taken together with the nitrogen atom is a 5-, 6-membered saturated heterocyclic moiety which optionally has a further hetero atom selected from the group consisting of S, N, and O, and can in turn be optionally substituted with, including on the further nitrogen atom, C_{1-3} alkyl, or C_{1-3} acyl;

wherein T is

a) O,

b) S, or

c) SO_2;

R_{75}, R_{76}, and R_{77} are the same as defined above;

R_{80} is

a) H,

b) formyl,

c) carboxyl,

d) C_{1-6} alkoxycarbonyl,

e) C_{1-8} alkyl,

f) C_{2-8} alkenyl,
wherein the substituents (e) and (f) can be optionally substituted with OH, halo, C_{1-6} alkoxy, C_{1-6} acyl, C_{1-6} alkylthio or C_{1-6} alkoxycarbonyl, or phenyl optionally substituted with halo,

g) an aromatic moiety having 6 to 10 carbon atoms optionally substituted with carboxyl, halo, -CN, formyl, CF_3, $-NO_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} acyl, C_{1-6} alkylthio, or C_{1-6} alkoxycarbonyl;

h) $-NR_{81}R_{82}$,

i) $-OR_{90}$,

j) $-S(=O)_i-R_{91}$,

k) $-SO_2-N(R_{92})(R_{93})$, or

l) a radical of the following formulas:

R_{81} and R_{82} at each occurrence are the same or different and are

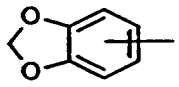
a) H,

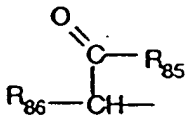
b) C_{3-6} cycloalkyl,

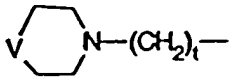
c) phenyl,

d) C_{1-6} acyl,

e) C_{1-6} alkyl optionally substituted with OH, C_{1-6} alkoxy which can be substituted with OH, a 5-, or 6-membered aromatic heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, phenyl optionally substituted with OH, CF_3, halo, $-NO_2$, C_{1-4} alkoxy, $-NR_{83}R_{84}$, or


;

f) 
, or

g) 
;

V is

a) O,

b) CH_2, or

c) NR_{87};

R_{83} and R_{84} at each occurrence are the same or different and are

a) H, or

b) C_{1-4} alkyl;

R_{85} is

a) OH,

b) C_{1-4} alkoxy, or

c) $-NR_{88}R_{89}$;

R_{86} is

a) H, or

b) C_{1-7} alkyl optionally substituted with indolyl, OH, mercaptyl, imidazoly, methylthio, amino, phenyl optionally substituted with OH, $-C(=O)-NH_2$, $-CO_2H$, or $-C(=NH)-NH_2$;

R_{87} is

a) H,

b) phenyl, or

c) C_{1-6} alkyl optionally substituted by OH;

R_{88} and R_{89} at each occurrence are the same or different and are

a) H,

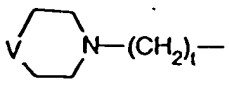
b) C_{1-5} alkyl

c) C_{3-6} cycloalky, or

d) phenyl;

R_{90} is

a) C_{1-8} alkyl optionally substituted with C_{1-6} alkoxy or C_{1-6} hydroxy, C_{3-6} cycloalkyl, a 6-membered aromatic optionally benzo-fused heterocyclic moiety having one to three nitrogen atoms, which can in turn be substituted with one or two $-NO_2$, CF_3, halo, -CN, OH, C_{1-5} alkyl, C_{1-5} alkoxy, or C_{1-5} acyl;

b) 

,

c) phenyl, or

d) pyridyl;

R_{91} is

a) C_{1-16} alkyl,

b) C_{2-16} alkenyl,

wherein the substituents (a) and (b) can be optionally substituted with C_{1-6} alkoxycarbonyl, or a 5-, 6-, 7-membered aromatic heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O,

c) an aromatic moiety having 6 to 10 carbon atoms, or

d) a 5-, 6-, 7-membered aromatic heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O,

wherein the substituents (c) and (d) can be optionally substituted with carboxyl, halo, -CN, formyl, CF_3, $-NO_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} acyl, C_{1-6} alkylthio, or C_{1-6} alkoxycarbonyl;

R_{92} and R_{93} at each occurrence are the same or different and are

a) H,

b) phenyl,

c) C_{1-6} alkyl, or

d) benzyl;

R_{94} and R_{95} at each occurrence are the same or different and are

a) H,

b) OH,

c) C_{1-6} alkyl optionally substituted with $-NR_{83}R_{84}$, or

d) R_{94} and R_{95} taken together are =O;

R_{96} is

a) an aromatic moiety having 6 to 10 carbon atoms,

b) a 5-, or 6-membered aromatic optionally benzo-fused heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O,

wherein the substituents (a) and (b) which can in turn be substituted with one or three $-NO_2$, CF_3, halo, -CN, OH, phenyl, C_{1-5} alkyl, C_{1-5} alkoxy, or C_{1-6} acyl,

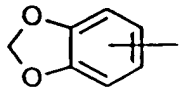
c) morpholinyl,

d) OH,

e) C_{1-6} alkoxy,

f) $-NR_{83}R_{84}$,

g) $-C(=O)-R_{97}$, or

h)  ;

R_{97} is

a) morpholinyl,

b) OH, or

c) C_{1-6} alkoxy;

h is 1, 2, or 3;

i is 0, 1, or 2;

j is 0 or 1;

k is 3, 4, or 5;

l is 2 or 3;

m is 4 or 5;

n is 0, 1, 2, 3, 4, or 5;

p is 0, 1, 2, 3, 4, or 5; with the proviso that n and p together are 1, 2, 3, 4, or 5;

q is 1, 2, 3, or 4;

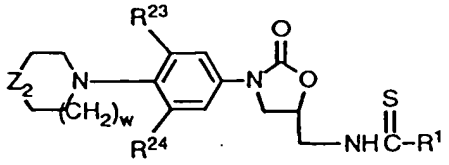
r is 2, 3, or 4;

t is 0, 1, 2, 3, 4, 5, or 6;

u is 1 or 2;

w is 0, 1, 2, or 3.

7. (amended) A method of treating or preventing osteoporosis, bone resorption, or other bone disease characterized by the need to enhance bone formation in a vertebrate mammal in need thereof comprising the administering to the vertebrate mammal an effective amount of a compound of formula II



(II)

wherein Z_2 is $-O_2S-$, $-O-$, $-N(R^{107})-$, $-OS-$, or $-S-$;

w is 0, 1, 2, or 3;

R^{23} and R^{24} are the same or different and can be H or F; and

R^1 is H, NH_2, NHalkylC_1-C_4; N(alkylC_1-C_4)$_2$;  :

alkylC_1-C_4; OalkylC_1-C_4; SalkylC_1-C_4; alkylC_1-C_4 substituted with 1-3F, 1-2Cl, CN, or -COOalkylC_1-C_4, or cycloalkylC_3-C_6, wherein in each occurrence of the alkyl group may be straight or branched; and

R^{107} is

a) $R^{102}O-C(R^{110})(R^{111})-C(O)-$,

b) $R^{103}O-C(O)-$,

c) $R^{108}-C(O)-$,

d) $R^{109}-SO_2-$,

e) $NC-CH_2-$,

f) $FCHCH_2-$, or

g) $R^{150}R^{151}NSO_2-$;

wherein R^{102} is H, CH_3-, phenyl-CH_2-, or $CH_3C(O)$; each of R^{110} and R^{111} is selected from H or CH_3; R^{103} is alkylC_1-C_3 or phenyl; R^{108} is H, alkylC_1-C_4, aryl$(CH_2)_{0-5}$, $CNCH_2$-, $ClCH_2$-, Cl_2HC-, FH_2C-, F_2HC-, or cycloalkylC_3-C_6; R^{150} and R^{151} are the same or different and are selected from H, alkylC_1-C_4, or R^{150} and R^{151} taken together with the nitrogen to which each is attached forms a monocyclic heterocyclic ring having from 3 to 6 carbon atoms.